Virginia Department of Health
Tularemia: Guidance for Health Care Providers
Key Medical and Public Health Interventions After Identification of a Suspected Case

1. Clinical Manifestations

Incubation period: Usually from 3-5 days. Range is 1-14 days.
Symptoms: Abrupt onset of illness with fever, headache, chills and rigors, generalized body aches (often prominent in the low back), and a sore throat. A dry or slightly productive cough and substernal pain or tightness frequently occurs with or without objective signs of pneumonia, such as purulent sputum, dyspnea, tachypnea, pleuritic pain, or hemoptysis. Nausea, vomiting, and diarrhea may occur.

Tularemia is characterized by several distinct forms:
A. Glandular: regional lymphadenopathy with no ulcer
B. Ulceroglandular: cutaneous ulcer with regional lymphadenopathy
C. Oculoglandular: conjunctivitis with preauricular lymphadenopathy
D. Oropharyngeal: stomatitis or pharyngitis or tonsillitis and cervical lymphadenopathy
E. Intestinal: intestinal pain, vomiting and diarrhea
F. Typhoidal: febrile illness without early localizing signs and symptoms
G. Pneumonic: primary pleuropulmonary disease

2. Identification and Isolation of Cases

Francisella tularensis as a bioterrorist agent: aerosol release in a densely populated area would likely result in large numbers of acute, nonspecific febrile illness beginning approximately 3 to 5 days later, with pleuropneumonitis developing in a significant proportion of cases in the following days. In addition to pleuropneumonitis, airborne release could infect the eye, resulting in oculoglandular tularemia; penetrate broken skin, resulting in ulceroglandular or glandular disease; or cause oropharyngeal disease with cervical lymphadenitis.

Isolation of tularemia patients is not recommended because tularemia is not directly transmitted from person to person. Contact precautions should be taken for open lesions.

3. Handling Laboratory Specimens

Laboratory personnel should be alerted when tularemia is suspected. Routine diagnostic procedures can be performed in biosafety level 2 conditions. Procedures that might produce aerosols or droplets should be conducted under biosafety level 3 conditions.

The Division of Consolidated Laboratory Services (DCLS) should be consulted before shipment of specimens. The DCLS Emergency Services Officer (ESO) can be reached 24 hours a day/7 days a week at 804-418-9923. Sample collection instructions are shown in Table 1.

Table 1. Sample Collection for Suspected Tularemia

Samples	*Amount*	*Type of Tularemia*	*Instructions*
Bronchial /tracheal wash or induced sputum	5-10 cc	Pneumonic	Collect in a sterile container and refrigerate.
Swab of eye	3-4 swabs	Oculoglandular	Send in bacterial transport media. Ship at room temperature.
Lymph node aspirate	1-2 cc	Glandular; Ulceroglandular	Ship to lab ASAP; if more than 2 hours, refrigerate.
Blood	10cc	Pneumonic (rarely a source of detection)	Blood isolator tube or aerobic blood culture bottle. Ship at room temperature. Transport to lab within 16 hours.
Serum	Acute and convalescent (14 days apart)	All	Collect in red top or tiger top tube. Remove serum and place in sterile tube, then store frozen.
Tissue: Biopsy of ulcer or wound; autopsy tissue	1 gram	Ulceroglandular, or any fatal case	Place in sterile container; moisten with sterile broth or saline. Ship to lab ASAP at room temperature. If more than 2 hours, freeze and ship on dry ice.
Bacterial isolate from culture			Ship suspicious isolates (tiny Gram-negative coccobacilli) on slant or agar plate at room temperature.

Additional laboratory guidance is available in the CDC publication *Level A Laboratory Procedures for Identification of Francisella tularensis*, available at: http://www.bt.cdc.gov/Agent/Tularemia/Tularemia.asp

4. Diagnosis

Clinical diagnosis is supported by evidence or history of an arthropod bite or exposure to infected aerosols or contaminated water, soil, vegetation, or animal tissues/fluids. *F. tularensis* may be identified through direct examination of secretions, exudates, or biopsy specimens using Gram-stain, direct fluorescent antibody, or immunohistochemical stains. Microscopic demonstration of *F. tularensis* using fluorescent-labeled antibodies is a rapid diagnostic procedure performed in designated reference laboratories. Growth of *F. tularensis* in culture (from pharyngeal washings, sputum specimens, or fasting gastric aspirates) is a definitive means of confirming the diagnosis. *F. tularensis* is only occasionally isolated from blood.

5. Treatment and Prophylaxis

If a known biological attack using *F. tularensis* has occurred and exposed persons are identified during the incubation period (before they become ill), then individuals should receive prophylactic treatment with 14 days of oral doxycycline or ciprofloxacin as outlined in Table 2. If an attack is discovered only after some individuals become ill, persons potentially exposed should begin surveillance for a fever. Those who develop an unexplained fever or flu-like illness within 14 days of presumed exposure should begin standard treatment as outlined in Table 2.

Post-exposure prophylactic treatment of close contacts of tularemia patients is not recommended because person-to-person transmission is not known to occur.

Laboratory personnel potentially exposed to the agent should be assessed on a case-by-case basis. For high-risk exposures (e.g. needle stick, spill, centrifuge accident), prophylaxis should be given. For other exposures, the health department should be consulted to assess the risk.

Treatment and prophylaxis recommendations are shown in Table 2.

Table 2. Working Group Consensus Recommendations for Treatment and Prophylaxis of Patients with Tularemia

Standard Treatment[1]	*Prophylaxis*[2] *Regimens in this column may also be used for treatment in severe circumstances when standard IM or IV treatment is impractical or unavailable.*
Adults (excluding pregnant women)	
Preferred Choices: Streptomycin, 1 g IM twice daily, or Gentamicin, 5mg/kg IM or IV once daily **Alternate Choices:** Doxycycline, 100mg IV twice daily, or Chloramphenicol, 15 mg/kg IV 4 times daily, or Ciprofloxacin, 400 mg IV twice daily	**Preferred Choices:** Doxycycline, 100 mg orally twice daily, or Ciprofloxacin, 500 mg orally twice daily
Pregnant Women	
Preferred Choices: Streptomycin, 1 g IM twice daily, or Gentamicin, 5mg/kg IM or IV once daily **Alternate Choices:** Doxycycline, 100 mg IV twice daily, or Ciprofloxacin, 400 mg IV twice daily	**Preferred Choices:** Doxycycline, 100 mg orally twice daily, or Ciprofloxacin, 500 mg orally twice daily
Children	
Preferred Choices: Streptomycin, 15mg/kg IM twice daily (should not exceed 2 gm/d), or Gentamicin, 2.5mg/kg IM or IV 3 times daily **Alternate Choices:** Doxycycline, If weight >= 45 kg, 100 mg IV If weight < 45 kg, give 2.2 mg/kg IV twice daily, or Chloramphenicol, 15mg/kg IV 4 times daily, or Ciprofloxacin, 15 mg/kg IV twice daily[3]	**Preferred Choices:** Doxycycline, If weight >=45 kg, give 100 mg orally twice daily If weight < 45 kg, give 2.2mg/kg orally twice daily, or Ciprofloxacin, 15 mg/kg orally twice daily[3]

[1] Treatment with streptomycin, gentamicin, or ciprofloxacin should be continued for 10 days; treatment with doxycycline or chloramphenicol should be continued for 14-21 days. Persons beginning treatment with IM or IV doxycycline, ciprofloxacin, or chloramphenicol can switch to oral antibiotics when clinically indicated.

[2] The duration of all recommended therapies for prophylaxis and treatment in severe circumstances when IM or IV treatment is not available is 14 days.

[3] Ciprofloxacin dosages should not exceed 1 g/d in children.

The US Food and Drug Administration has not approved all treatment regimens shown in the chart.

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6. Decontamination

Persons with direct exposure to powder or liquid aerosols containing *F. tularensis* should wash body surfaces with soapy water. Standard levels of chlorine in water should protect against waterborne infection. Clothing or linens contaminated with body fluids of patients with tularemia should be disinfected per standard hospital procedure.

Following an intentional release of *F. tularensis*, the risk to humans of acquiring tularemia from infected animals or arthropod bites is considered minimal and could be reduced by avoidance of sick or dead animals and by using protective measures against biting arthropods.

7. Postmortem Practices

If tularemia is suspected as a cause of death, the regional office of the state medical examiner should be immediately notified. Bodies of patients who die of tularemia should be handled using standard precautions, but autopsy procedures likely to produce aerosols or droplets should be avoided.

8. Public Health Measures

A. Suspected cases should be reported to hospital epidemiology/infection control, who in turn should notify laboratory personnel, other medical care providers and public health.
B. Arrange for laboratory testing by consulting with public health or the DCLS at 804-418-9923 (24 hour/7 day).
C. Designated public health authority should begin an epidemiologic investigation immediately, including fever surveillance of individuals potentially exposed to *F. tularensis*.

Information excerpted from:
Dennis DT; Inglesby TV; Henderson DA, et al. Tularemia as a Biological Weapon: Medical and Public Health Management. *JAMA*. 2001;285(21):2763-2773.